Serial No.: 09/927,160

Filed: August 9, 2001

On page 100, immediately preceding the heading "CLAIMS", please insert the enclosed text entitled "SEQUENCE LISTING."

## **REMARKS**

The specification has been amended to include a Sequence Listing and proper reference to the sequences therein. Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

Entry of this amendment is respectfully requested. The amendments are made in adherence with 37 C.F.R. § 1.821-1.825. This amendment is accompanied by a floppy disk containing the above named sequence, SEQUENCE ID NUMBERS 1-12 in computer readable form, and a paper copy of the sequence information. The computer readable sequence listing was prepared through use of the software program "PatentIn" provided by the PTO. The information contained in the computer readable disk is identical to that of the paper copy. This amendment contains no new matter. Applicant submits that this amendment, the accompanying computer readable sequence listing, and the paper copy thereof serve to place this application in a condition of adherence to the rules 37 C.F.R. § 1.821-1.825.

-5-1064586

**Serial No.**: 09/927,160 **Filed**: August 9, 2001

Please direct any calls in connection with this application to the undersigned at (415) 781-1989.

Respectfully submitted,

FLEHR HOHBACH TEST ALBRITTON & HERBERT LLP

Dated: October 15 2001

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**Serial No.**: 09/927,160 **Filed**: August 9, 2001

## **VERSION WITH MARKINGS TO SHOW CHANGES MADE**

## **IN THE SPECIFICATION:**

Paragraph beginning at page 14, line 5, has been amended as follows:

- Fig. 5. PCR products and primers (SEQ ID NOS:1-3) from the lacZ (β-galactosidase) gene sequence. The location of the 11 bp Xba linker (SEQ ID NO:4) is shown.-

Paragraph beginning at page 20, line 15, has been amended as follows:

– Figs. 20A and 20B. The organization of the mouse OTC gene. Sequence of cssDNA probes and PCR primers used in this study are indicated (SEQ ID NO:5). Sizes of the exons in base pairs are indicated. The relative position of PCR primers M9, M8 and M11 are shown. B) Map of plasmid pTAOTC1. A 250 bp fragment containing the normal OTC exon 4 sequence and surrounding introns were cloned into the EcoRV site of pbluescript SK (+) (Stratagene).—

Paragraph beginning at page 20, line 21, has been amended as follows:

- Fig. 21. Sequence analysis of exon 4 of the mouse OTC gene in founder mice. PCR amplification of genomic DNA from tail biopsies of a pool of all of the homozygous (spf-ash/spf-ash) females used as egg donors and each indicated individual founder mice were sequenced using cycle sequencing with the M11 primer (Cyclist kit, Stratagene). The DNA sequence surrounding the spf-ash locus (arrow) in the OTC gene is shown (SEQ ID NO:6).-

1064586 -7-

Serial No.: 09/927,160

Filed: August 9, 2001

Paragraph beginning at page 69, line 1, has been amended as follows:

- The plasmid pMC1lacpA (8.4 kb) contains the strong polyoma virus promoter of

transcription plus ATG placed in front of the lacZ gene. The polyadenylation signal from

SV40 virus was placed in back of the lacZ gene. The plasmid vector was pIB130 from

IBI (New Haven, CT). The mutant vector pMC1lacpA has a 11-bp insertion in the XbaI

site consisting of the inserted sequence CTCTAGACGCG (see Figure 5; SEQ ID

NO:4).-

Paragraph beginning at page 69, line 11, has been amended as follows:

- We synthesized two 20-bp primers (PCRα and PCRβ; SEQ ID NOS:2 &3) for

producing a 276-bp PCR product (see Figure 5) from the wild-type lacZ sequence for use

as targeting polynucleotides. We chose this 276-bp fragment to span the 11 bp insertion

mutation as a nonhomologous sequence. The 276-bp DNA oligonucleotide was separated

by gel electrophoresis and electroeluted from agarose, ethanol precipitated, and its

concentration determined by absorbance at 260 nm. The 276-bp fragment was 5' end-

labeled with <sup>32</sup>P and specifically D-looped with the pMc1lacXpA or pMC1lacpA plasmid

DNA using recA as shown by agarose gel electrophoresis.—

Paragraph beginning at page 78, line 23, has been amended as follows:

- CF1

S

5'-GCAGAGTACCTGAAACAGGA (SEQ ID NO:7)-

Paragraph beginning at page 78, line 24, has been amended as follows:

-8-1064586

**Serial No.**: 09/927,160 **Filed**: August 9, 2001

- CF5 Α 5'-CATTCACAGTAGCTTACCCA (SEQ ID NO:8)-Paragraph beginning at page 78, line 25, has been amended as follows: - CF6 5'-CCACATATCACTATATGCATGC (SEQ ID NO:9)-A Paragraph beginning at page 78, line 28, has been amended as follows: - CF17 S 5'-GAGGGATTTGGGGAATTATTTG (SEQ ID NO:10)-Paragraph beginning at page 78, line 29, has been amended as follows: - OLITGO N Α 5'-CACCAAAGATGATATTTTC (SEQ ID NO:11)-Paragraph beginning at page 80, line 1, has been amended as follows: - OLIGO ΔF Α 5'-AACACCAAGATATTTCTT (SEQ ID NO:12)-

On page 100, immediately preceding the claims, the enclosed Sequence Listing was added to the text.